Remarks/Arguments:

1. In the Office Action mailed May 17, 2004, claims 1-8 and 20 remain pending. Claim 1 is currently being amended herein and claims 2 and 3 are currently being cancelled herein. As discussed in the telephone conversation between Examiner Cook and the undersigned on August 31, 2004, Applicants now submit an amendment and remarks/arguments addressing the Kitagawa et al. reference (EMBO 15: 7060-7069, 1996) (hereinafter "Kitagawa") which was first raised by the Examiner in the final rejection mailed May 17, 2004. In the above-referenced telephone conversation, Examiner Cook said that she would consider the amendment and remarks/arguments now submitted by Applicants.

2. Claim 1 is currently amended to recite an assay for CDK2 activity using a capture antibody that specifically recognizes Rb protein phosphorylated at residue Ser249, Thr252, Thr356, Ser612, Ser807, Ser811, or Thr821. As the Examiner will appreciate, support for this amendment is found in original claim 2, and in the specification's description, as originally filed, for example, at page 4, lines 19-22, and at page 6, lines 18-24. Accordingly, no new matter is being added by this amendment.

3. Claims 1-7, and 20 stand rejected, under 35 U.S.C. § 103, for obviousness over Wen et al. (hereinafter "Wen") in view of Juan et al. (hereinafter "Juan"), and further in view of Watanabe. Applicants believe that the claims, as now being amended, are allowable over the cited art.

As noted in Applicants' remarks/arguments filed in the amendment dated January 29, 2004, Wen is merely an assay for detecting total Rb. Wen does not disclose or suggest the specific Rb residues targeted for assessment of CDK2 activity by the present invention. Furthermore, Wen neither discloses nor suggests the existence of the CDK2 "capture antibodies" used in the presently claimed invention which specifically recognize Rb phosphorylated at these specific CDK2-mediated residues. Wen, also, neither discloses nor suggests that such antibodies could be successfully used to capture CDK2-phosphorylated Rb as a means of assessing CDK2 activity in combination with an anti-Rb antibody. In contrast, Wen uses two different antibodies that recognize Rb in a phosphorylation-independent manner to measure total Rb.

The deficiencies of Wen are not cured by Juan. Juan discloses an assay for monitoring Rb phosphorylation by incubating cells with dual fluorochrome-tagged antibodies. While one antibody assesses total Rb, a second antibody is specific for underphosphorylated Rb. Rb phosphorylation is assessed by comparing the dual

fluorochrome signals that represent either total Rb or underphosphorylated Rb. With respect to the phosphorylation-dependent antibody, Juan discloses an antibody completely distinct from the "capture antibody" of the presently claimed invention. The Juan phosphorylation-related antibody recognizes an underphosphorylated Rb, rather than the specifically CDK2-phosphorylated Rbs recognized by the capture antibody of the present claimed invention. Furthermore, Juan discusses antibodies used to measure dual readouts rather than a single readout in an ELISA-based dual antibody-complex assay. The presently claimed invention, rather than relying on dual readouts to assess the CDK2-mediated Rb phosphorylation, directly measures only the second anti-Rb primary antibody. This is correlated with, but not a direct measure of, the capture antibody present because the only Rb present for the anti-Rb primary antibody to measure is indeed CDK2-phosphorylated Rb following isolation of the capture antibody-Rb complex from the remainder of the sample, as recited in Claim 1, step (ii).

Either alone, or in combination with the above-discussed Wen, Juan in no way discloses or suggests that Rb is phosphorylated by CDK2 at the residues recognized by the capture antibodies of the presently claimed invention, that antibodies specific for detecting CDK2 at these residues exist or can be made, or that such antibodies could be successfully used as a capture antibody, in combination with an anti-Rb primary antibody, as in the presently claimed invention, to detect CDK2 phosphorylation at these specific sites using an ELISA-based format.

Applicants respectfully remind the Examiner that Watanabe is not properly available to support a prior art rejection. Applicants have successfully sworn behind this reference (see Declaration, under 37 C.F.R. § 1.131, by co-inventors Barbara A. Foster and Farzan Rastinejad, filed May 5, 2003, and the supporting document attesting to this Declaration, filed January 29, 2004). To the extent that Kitagawa (a reference cited by Watanabe) is relied upon to support this rejection based upon disclosure of phospho-specific Rb antibodies, Applicant notes that Kitagawa merely discloses the use of the Ser780 phospho-specific anti-Rb antibody, where the Ser780 is a residue phosphorylated by only CDK4 but not by CDK2. Thus, Kitagawa, either alone or in combination with Wen or Juan, fails to disclose or suggest the claimed CDK2 activity assay, as presently claimed, because there is no disclosure or suggestion of the existence of CDK2 phospho-specific anti-Rb antibodies or that such antibodies could be successfully made, or that such antibodies could successfully be used as capture antibodies in a CDK2 ELISA-based format. Therefore, Applicants respectfully